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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER
GRUMBLING, M

ART UNIT	PAPER NUMBER
122	6

DATE MAILED: 07/09/91

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☑ This application has been examined ☑ Responsive to communication filed on 5/6/1991 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☑ Claims 1-16 are pending in the application.
   Of the above, claims 4-12 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-3 and 13-16 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

Applicant's election without traverse of invention I, claims 1-3 and 13-16 in Paper No. 5, filed on the 6th of May, 1991 is acknowledged.

The Abstract of the Disclosure is objected to because the abstract should contain definitions of all substituents which are presented therein or, in the alternative, indicate that the substituents are identified in the body of the specification. Correction is required. See M.P.E.P. § 608.01(b).

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

On page 2, line 19: should "sue" be "use"? On 13, line 14 should "[produce]" be "product"?

To insure proper consideration, applicant should provide the examiner with a copy of the foreign art cited in the specification because it is not readily available to the examiner.

Specifically, a copy of Mei et al. should be provided along with an explanation of how the article relates to the invention and how the procedure described in the article demonstrates utility of the invention.

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new

> and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 14 and 16 are rejected under 35 U.S.C. § 101 because the specification teaches a specific medicinal use on humans, i.e. treatment of asthma, however, no evidence has been presented that the claimed method would possess that utility in humans.

Proof of medicinal utility on humans is required unless one of ordinary skill in the art would accept the utility as obviously valid.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure.

The specification is drawn to methods of treating local inflammation while reducing systemic effects of corticosteroids. Since the specification mentions bronchial asthma as one type of inflammation to be treated, it is assumed that humans use is contemplated as within the scope of the methods of use claims. Proof of human utility is required unless it can be shown that one of ordinary skill in the art would accept the utility as

obviously valid.

Claims 14 and 16 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

In addition to the above rejection, the following questions arise in reading the specification: In Table II, compounds of the instant invention are presented, yet R_2 is not defined for compounds 7-9 and 13-15. Is R_2 assumed to be H in these cases or is it supposed to be something else? If the latter, what?

It is noted that the examples present evidence of utility for only the 16, 17 pentilidynebis(oxy) product although other products are clearly made and claimed. Is this intentional? Are compounds 7-9 or 13-15 supposed to be the cyclohexylmethylidyne bis(oxy) products? Some other product?

Claims 13-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 refers to the "composition of claim 1", however, claim 1 is a compound claim thus claim 13 lacks antecedent basis in the base claim from which it depends. Note that a composition is considered a mixture of two or more substances.

Claim 15, likewise lacks antecedent basis in the base claim from which it depends.

As written, claims 13 and 15 merely reiterate the elements of claim 1 and thus are unnecessarily redundant.

Claim 14 is a nonstatutory claim. Is this meant to be a method of use claim? The limitations of the claim, i.e. "Low systemic effect", etc. are vague because they cannot be quantated and are impossible to interpret. Perhaps the claim should be written as a method of treating inflammation while minimizing systemic glucocorticoid effect comprising administering an antiinflammatorilly effective amount of a compound according to claim 1.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1 and 13-16 are rejected under 35 U.S.C. § 103 as being unpatentable over Brattsand et al. (A). The claims are drawn to compounds, compositions and methods of use wherein the compounds are 21-esters of 16, 17-methylene dioxy steroids. The claimed compounds wherein R_1 is lower alkyl and R_2 is lower acetyl are structurally similar to those generically taught by Brattsand et al. Specifically when R_1 is butyl and R_2 is acetyl, the claimed compound is the next adjacent homolog to example 16 presented in Table 4 in column 5 of Brattsand et al. In addition, Brattsand et al. teach antiinflammatory use of those compounds.

The claimed compounds, compositions and methods of use would have been obvious to one of ordinary skill in the art at the time the invention was made because the claimed compounds are structurally related compounds which would be expected to have similar chemical and pharmaceutical properties and because one of ordinary skill in the art would make and use the compounds of Brattsand et al. as a matter of preference depending on factors (such as cost and availability of starting materials) not related to pharmaceutical properties.

Claims 1-3 and 13-16 are rejected under 35 U.S.C. § 103 as being unpatentable over Brattsand et al. (A) as applied above in

view of Brattsand et al. (B). The claimed compounds, compositions and methods of use comprise 21-esterified 2-alkylated-16, 17-methylene dioxy steroids very similar to those taught by Brattsand et al. (A). Specifically, the compound of Example 16 in Table 4 at column 5 of Brattsand et al. (A) is the next adjacent homolog to the claimed (racemic) compound wherein R_1 is butyl and R_2 is acetyl. Brattsand (A) does not teach of the isomerism at the Z^1 position.

Brattsand et al. (B) teaches isolation of steroisomers of compounds structurally similar to those of Brattsand (A) and the claimed compounds. Moreover, Brattsand (B) teaches that such isolation is desirable because the stereoisomer has "consistently physiologically better characteristics" than the other stereoisomer. (at Col. 2, lines 7-19). The compounds of Brattsand (B) are also antiinflammatory.

It would have been obvious to make and use the claimed compounds and compositions as antiinflammatories at the time the invention was made because the claimed compounds have structures very similar to those of Brattsand et al. (A) and (B) and would be expected to have very similar properties and because Brattsand et al. (B) further motivates making and use of enantiomerically pure compounds and compositions of steroids which are structurally (and presumably pharmaceutically) similar to those of Brattsand et al. (A) and the claimed compounds.

MacDonald and Diassi et al. are cited as further defining state of the corticosteroid art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Grumbling whose telephone number is (703) 308-4713.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Mukund J. Shah

SUPERVISORY PATENT EXAMINER
GROUP 120

Grumbling: ach
July 08, 1991

MJS